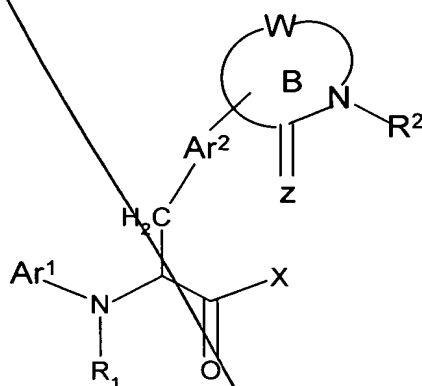


5

WHAT IS CLAIMED IS:

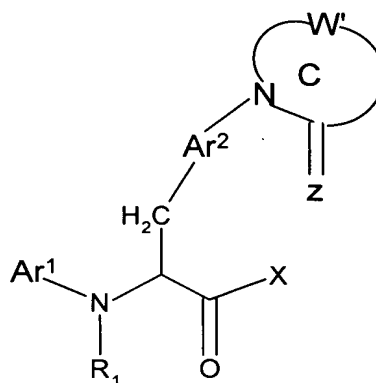
1. A compound (Ia) or (Ib):

10



(Ia)

or



(Ib)

wherein:

Ar<sup>1</sup> is an aryl, heteroaryl, cycloalkyl, or heterocyclic group wherein said aryl, heteroaryl, cycloalkyl, or heterocyclic group is optionally substituted, on any ring atom capable of substitution, with 1-3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, acyl, acylamino, thiocarbonylamino, acyloxy, amino, substituted amino, amidino, alkyl amidino, thioamidino, aminoacyl, aminocarbonylamino, aminothiocarbonylamino, aminocarbonyloxy, aryl, substituted aryl, aryloxy, substituted aryloxy, aryloxyaryl, substituted aryloxyaryl, cyano, halogen, hydroxyl, nitro, oxo, carboxyl, cycloalkyl, substituted cycloalkyl, guanidino, guanidinosulfone, thiol, thioalkyl, substituted thioalkyl, thioaryl, substituted thioaryl, thiocycloalkyl, substituted thiocycloalkyl, thioheteroaryl, substituted thioheteroaryl, thioheterocyclic, substituted thioheterocyclic, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, cycloalkoxy, substituted cycloalkoxy, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy, substituted heterocyclyloxy, oxycarbonylamino, oxythiocarbonylamino, -OS(O)<sub>2</sub>-alkyl, -OS(O)<sub>2</sub>-substituted alkyl, -OS(O)<sub>2</sub>-

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5 aryl, -OS(O)<sub>2</sub>-substituted aryl, -OS(O)<sub>2</sub>-heteroaryl, -OS(O)<sub>2</sub>-substituted  
heteroaryl, -OS(O)<sub>2</sub>-heterocyclic, -OS(O)<sub>2</sub>-substituted heterocyclic, -OSO<sub>2</sub>-  
NRR where each R is independently hydrogen or alkyl, -NRS(O)<sub>2</sub>-alkyl, -  
NRS(O)<sub>2</sub>-substituted alkyl, -NRS(O)<sub>2</sub>-aryl, -NRS(O)<sub>2</sub>-substituted aryl, -  
NRS(O)<sub>2</sub>-heteroaryl, -NRS(O)<sub>2</sub>-substituted heteroaryl, -NRS(O)<sub>2</sub>-heterocyclic,  
10 -NRS(O)<sub>2</sub>-substituted heterocyclic, -NRS(O)<sub>2</sub>-NR-alkyl, -NRS(O)<sub>2</sub>-NR-  
substituted alkyl, -NRS(O)<sub>2</sub>-NR-aryl, -NRS(O)<sub>2</sub>-NR-substituted aryl, -  
NRS(O)<sub>2</sub>-NR-heteroaryl, -NRS(O)<sub>2</sub>-NR-substituted heteroaryl, -NRS(O)<sub>2</sub>-NR-  
heterocyclic, -NRS(O)<sub>2</sub>-NR-substituted heterocyclic where R is hydrogen or  
alkyl, -N[S(O)<sub>2</sub>-R']<sub>2</sub> and -N[S(O)<sub>2</sub>-NR']<sub>2</sub> where each R' is independently  
15 selected from the group consisting of alkyl, substituted alkyl, aryl, substituted  
aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted  
heterocyclic;

R<sup>1</sup> is selected from the group consisting of hydrogen, alkyl, substituted  
alkyl, alkenyl, substituted alkenyl, cycloalkyl, substituted cycloalkyl,  
20 cycloalkenyl, substituted cycloalkenyl, aryl, substituted aryl, heteroaryl,  
substituted heteroaryl, heterocyclic and substituted heterocyclic;

Ar<sup>2</sup> is an aryl or heteroaryl group optionally substituted, in addition to  
ring B or C, with one or two substituent(s) selected from the group consisting  
of hydrogen, halogen, hydroxy, alkoxy, substituted alkoxy, acyloxy, amino,  
25 alkylamino, substituted alkylamino, dialkylamino, substituted dialkylamino,  
acylamino, aminoacyl, N-acyl-N-alkylamino, substituted N-acyl-N-  
alkylamino, (alkylsulfonyl)amino, substituted (alkylsulfonyl)amino, N-  
(alkylsulfonyl)-N-alkylamino, substituted N-(alkylsulfonyl)-N-alkylamino,  
alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted  
30 alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl,  
cyano, acyl, substituted acyl, carboxy, substituted carboxy, thiol, alkylthio,  
substituted alkylthio, alkylsulfoxy, substituted alkylsulfoxy, alkylsulfonyl,  
and substituted alkylsulfonyl;

Z is -O- or -S-;

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5 B is a group wherein W, together with  $-C(=Z)NR^2-$ , forms a saturated or  
unsaturated heterocyclic group containing 2 to 5 carbon atoms and 0 to 4  
additional heteroatoms selected from the group consisting of nitrogen,  
oxygen, and  $-SO_n-$  (where n is 0 to 2) wherein said saturated or unsaturated  
heterocyclic group is optionally fused with one or two ring(s) structures  
10 selected from the group consisting of cycloalkyl, cycloalkenyl, heterocyclic,  
aryl and heteroaryl group to form a bi- or tri-fused ring system and further  
wherein said heterocyclic group and each of such ring structures are  
optionally substituted with 1 to 3 substituents selected from the group  
consisting of with one or two substituent(s) selected from the group consisting  
15 of hydrogen, halogen, hydroxy, alkoxy, substituted alkoxy, acyloxy,  
substituted acyloxy, amino, alkylamino, substituted alkylamino, dialkylamino,  
substituted dialkylamino, acylamino, substituted acylamino, N-acyl-N-  
alkylamino, substituted N-acyl-N-alkylamino, alkylene dioxy,  
(alkylsulfonyl)amino, substituted (alkylsulfonyl)amino, N-(alkylsulfonyl)-N-  
20 alkylamino, substituted N-(alkylsulfonyl)-N-alkylamino, alkyl, substituted  
alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl,  
cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, cyano,  
acyl, substituted acyl, carboxy, substituted carboxy, nitro, thiol, alkylthio,  
substituted alkylthio, alkylsulfoxy, substituted alkylsulfoxy, alkylsulfonyl,  
25 substituted alkylsulfonyl, aryl, substituted aryl, heteroaryl, substituted  
heteroaryl;

R<sup>2</sup> is selected from the group consisting of alkyl, substituted alkyl, aryl,  
substituted aryl, heteroaryl, substituted heteroaryl, cycloalkyl, substituted  
cycloalkyl, cycloalkenyl, and substituted cycloalkenyl;

30 C is a group wherein W', together with  $-C(=Z)N-$ , forms a saturated or  
unsaturated heterocyclic group containing 2 to 5 carbon atoms and 0 to 4  
additional heteroatoms selected from the group consisting of nitrogen,  
oxygen, and  $-SO_n-$  (where n is 0 to 2) wherein said saturated or unsaturated  
heterocyclic group is optionally fused with one or two ring(s) structures

Sub  
A'

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5 selected from the group consisting of cycloalkyl, cycloalkenyl, heterocyclic,  
aryl and heteroaryl group to form a bi- or tri-fused ring system and further  
wherein said heterocyclic group and each of such ring structures are  
optionally substituted with 1 to 3 substituents selected from the group  
consisting of with one or two substituent(s) selected from the group consisting  
10 of hydrogen, halogen, hydroxy, alkoxy, substituted alkoxy, alkylendioxy,  
acyloxy, substituted acyloxy, amino, alkylamino, substituted alkylamino,  
dialkylamino, substituted dialkylamino, acylamino, substituted acylamino, N-  
acyl-N-alkylamino, substituted N-acyl-N-alkylamino, (alkylsulfonyl)amino,  
substituted (alkylsulfonyl)amino, N-(alkylsulfonyl)-N-alkylamino, substituted  
15 N-(alkylsulfonyl)-N-alkylamino, alkyl, substituted alkyl, cycloalkyl,  
substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted  
cycloalkenyl, alkynyl, substituted alkynyl, cyano, nitro, acyl, substituted  
acyl, carboxy, substituted carboxy, thiol, alkylthio, substituted alkylthio,  
alkylsulfoxy, substituted alkylsulfoxy, alkylsulfonyl, substituted  
20 alkylsulfonyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl;

X is selected from the group consisting of hydroxyl, alkoxy,  
substituted alkoxy, alkenoxy, substituted alkenoxy, cycloalkoxy, substituted  
cycloalkoxy, cycloalkenoxy, substituted cycloalkenoxy, aryloxy, substituted  
aryloxy, heteroaryloxy, substituted heteroaryloxy, heterocycloxyloxy,  
25 substituted heterocycloxyloxy and -NR<sup>''</sup>R<sup>''</sup> where each R<sup>''</sup> is independently  
selected from the group consisting of hydrogen, alkyl, substituted alkyl,  
alkenyl, substituted alkenyl, cycloalkyl, substituted cycloalkyl, aryl,  
substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and  
substituted heterocyclic;

30 and enantiomers, diastereomers and pharmaceutically acceptable salts  
thereof;

and further wherein the compound of Formula I has a binding affinity to  
VLA-4 as expressed by an IC<sub>50</sub> of about 15 μM or less.

Sub  
A<sup>1</sup>

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Sub  
A'

5 2. The compound of Claim 1 wherein (Ia), B is a group wherein W,  
together with  $-C(=Z)NR^2-$  where Z is  $-O-$ , forms an unsaturated heterocyclic  
group containing 2 to 4 carbon atoms and 0 to 2 additional nitrogen atoms and  
further the wherein the unsaturated heterocyclic group is optionally  
substituted, in addition to the  $R^2$  group, with 1 or 2 substituents selected from  
10 the group consisting of alkyl, alkoxy, substituted alkoxy, alkenyloxy,  
substituted alkenyloxy, halo, hydroxy, mono or dialkylamino.

15 3. The compound of Claim 1 wherein B is 2-pyridon-3-yl, 2-pyridon-4-yl,  
or 6-pyrimidon-5-yl that is optionally substituted, in addition to the  $R^2$  group,  
with 1 or 2 substituents selected from the group consisting of alkyl, alkoxy,  
substituted alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono  
or dialkylamino.

20 4. The compound of Claim 1 wherein B is a group wherein W, together  
with  $-C(=Z)NR^2-$  where Z is  $-O-$ , forms a saturated or unsaturated  
heterocyclic group containing 2 to 4 carbon atoms and 0 to 2 additional  
nitrogen atoms wherein said saturated or unsaturated heterocyclic group is  
fused to a heterocyclic ring selected from the group consisting of dioxolane,  
dioxane, homodioxane, oxetane, tetrahydrofuran, dihydropyran, furan,  
25 oxazolidine, oxazole, isoxazole, oxazolidinone, oxathiolane, and 1,3-  
dioxolan-2-one and wherein the resulting fused ring is optionally substituted,  
in addition to the  $R^2$  group, on any ring atom capable of substitution with 1 or  
2 substituents selected from the group consisting of alkyl, alkoxy, substituted  
alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or  
30 dialkylamino.

5. The compound of Claim 1 wherein B is 2-pyridone or 6-pyrimidone that  
is fused to a heterocyclic ring selected from the group consisting of  
dioxolane, dioxane, homodioxane, oxetane, tetrahydrofuran, dihydropyran,

5 furan, oxazolidine, oxazole, isoxazole, oxazolidinone, oxathiolane, and 1,3-  
dioxolan-2-one, and wherein the resulting fused ring is optionally substituted,  
in addition to the  $R^2$  group, on any ring atom capable of substitution with 1 or  
2 substituents selected from the group consisting of alkyl, alkoxy, substituted  
10 alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or  
dialkylamino.

15 6. The compound of Claim 1 wherein  $Ar^1$  is heteroaryl optionally  
substituted with 1 to 3 substituents selected from the group consisting of  
alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino,  
cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl,  
substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen.

20 7. The compound of Claim 6 wherein  $Ar^1$  is 1-oxo-1,2,5-thiadiazole, 1,1-  
dioxo-1,2,5-thiadiazole, pyridazine, pyrimidine or pyrazine ring which is  
optionally substituted with 1 to 3 substituents selected from the group  
consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino,  
substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl,  
heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and  
25 halogen.

8. The compound of Claim 2 to 7 wherein  $Ar^2$  is phenyl.

9. The compound of Claim 1 to 7 wherein X is hydroxyl and  $R^1$  is  
hydrogen.

10. The compound of Claim 8 wherein X is hydroxyl and  $R^1$  is hydrogen.

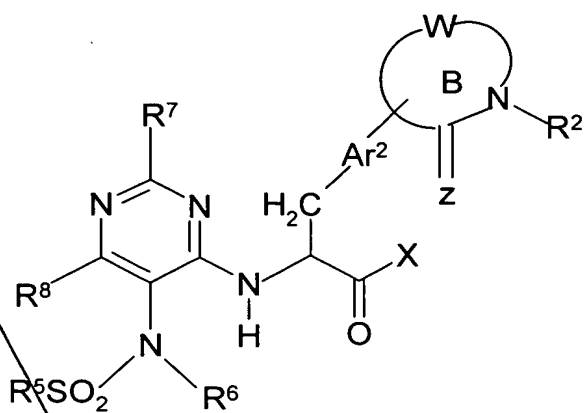
11. The compound of Claim 1 wherein the compound has formula IIa, IIb,  
IIc, IId, or IIe:

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A2

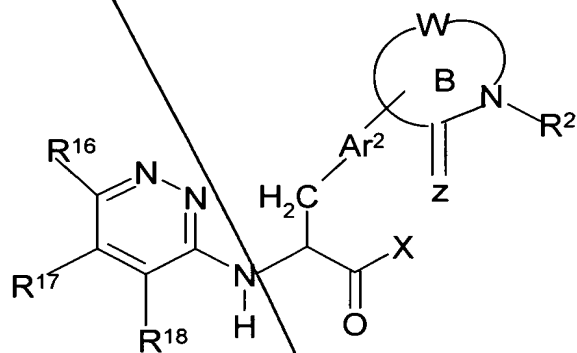
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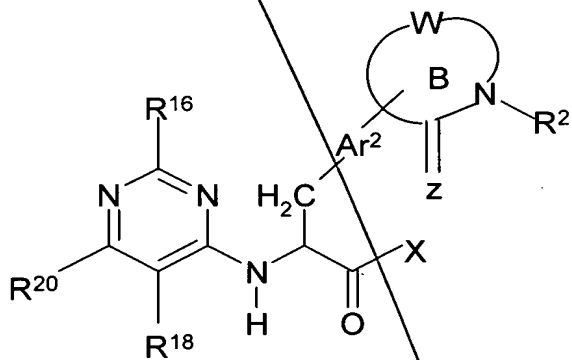
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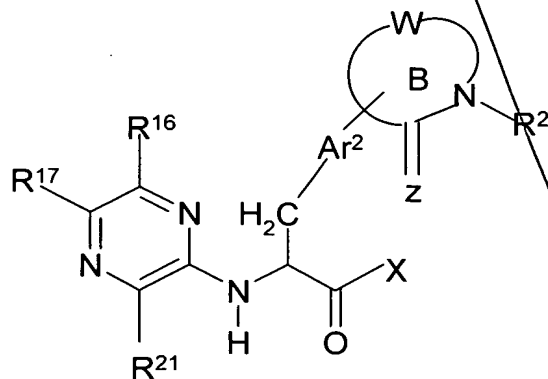
IIa



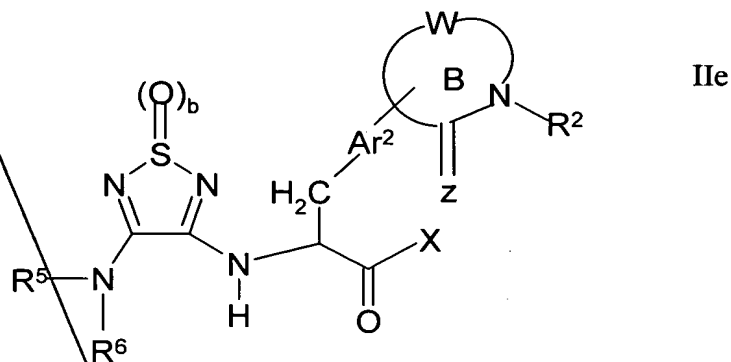
IIb



IIc



IIId



wherein

X is hydroxyl or alkoxy;

Ar<sup>2</sup> is an aryl or heteroaryl group optionally substituted, in addition to ring B or C, with one or two substituent(s) selected from the group consisting of hydrogen, halogen, hydroxy, alkoxy, substituted alkoxy, acyloxy, substituted acyloxy, amino, alkylamino, substituted alkylamino, dialkylamino, substituted dialkylamino, acylamino, substituted acylamino, N-acyl-N-alkylamino, substituted N-acyl-N-alkylamino, (alkylsulfonyl)amino, substituted (alkylsulfonyl)amino, N-(alkylsulfonyl)-N-alkylamino, substituted N-(alkylsulfonyl)-N-alkylamino, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, cyano, acyl, substituted acyl, carboxy, substituted carboxy, thiol, alkylthio, substituted alkylthio, alkylsulfoxy, substituted alkylsulfoxy, alkylsulfonyl, and substituted alkylsulfonyl;

R<sup>5</sup> is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, heteroaryl and substituted heteroaryl;



5             $R^6$  is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and  $-SO_2R^{10}$  where  $R^{10}$  is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl;

10             $R^7$  and  $R^8$  are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

15             $R^{16}$  and  $R^{17}$  are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen; and

20             $R^{18}$  is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

25             $R^{20}$  is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

30             $R^{21}$  is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclic and substituted heterocyclic;

$b$  is 1 or 2; and

$B$  is a group wherein  $W$ , together with  $-C(=Z)NR^2-$ , forms a saturated or unsaturated heterocyclic group containing 2 to 5 carbon atoms and 0 to 4

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A<sup>2</sup>

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5 additional heteroatoms selected from the group consisting of nitrogen,  
oxygen, and  $-SO_n-$  (where n is 0 to 2) wherein said saturated or unsaturated  
heterocyclic group is optionally fused with one or two ring(s) structures  
selected from the group consisting of cycloalkyl, cycloalkenyl, heterocyclic,  
aryl and heteroaryl group to form a bi- or tri-fused ring system and further  
10 wherein said heterocyclic group and each of such ring structures are  
optionally substituted with 1 to 3 substituents selected from the group  
consisting of with one or two substituent(s) selected from the group consisting  
of hydrogen, halogen, hydroxy, alkoxy, substituted alkoxy, acyloxy,  
substituted acyloxy, amino, alkylamino, substituted alkylamino, dialkylamino,  
15 substituted dialkylamino, acylamino, substituted acylamino, N-acyl-N-  
alkylamino, substituted N-acyl-N-alkylamino, alkylene dioxy,  
(alkylsulfonyl)amino, substituted (alkylsulfonyl)amino, N-(alkylsulfonyl)-N-  
alkylamino, substituted N-(alkylsulfonyl)-N-alkylamino, alkyl, substituted  
alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl,  
20 cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, cyano,  
acyl, substituted acyl, carboxy, substituted carboxy, nitro, thiol, alkylthio,  
substituted alkylthio, alkylsulfoxy, substituted alkylsulfoxy, alkylsulfonyl,  
substituted alkylsulfonyl, aryl, substituted aryl, heteroaryl, substituted  
heteroaryl;

25  $R^2$  is selected from the group consisting of alkyl, substituted alkyl, aryl,  
substituted aryl, heteroaryl, substituted heteroaryl, cycloalkyl, substituted  
cycloalkyl, cycloalkenyl, and substituted cycloalkenyl; and  
and enantiomers, diastereomers and pharmaceutically acceptable salts  
thereof.

30  
12. The compound of Claim 11 wherein the compound is selected from  
formula IIc, IId or IIe.

5W<sub>3</sub>  
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5 13. The compound of Claim 11 wherein B is a group wherein W, together  
with -C(=Z)NR<sup>2</sup>- where Z is -O-, forms an unsaturated heterocyclic group  
containing 2 to 4 carbon atoms and 0 to 2 additional nitrogen atoms and  
further the wherein the unsaturated heterocyclic group is optionally  
substituted, in addition to the R<sup>2</sup> group, with 1 or 2 substituents selected from  
10 the group consisting of alkyl, alkoxy, substituted alkoxy, alkenyloxy,  
substituted alkenyloxy, halo, hydroxy, mono or dialkylamino.

15 14. The compound of Claim 13 wherein B is 2-pyridon-3-yl, 2-pyridon-4-yl,  
or 6-pyrimidon-5-yl that is optionally substituted, in addition to the R<sup>2</sup> group,  
with 1 or 2 substituents selected from the group consisting of alkyl, alkoxy,  
substituted alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono  
or dialkylamino.

20 15. The compound of Claim 11 wherein B is a group wherein W, together  
with -C(=Z)NR<sup>2</sup>- where Z is -O-, forms a saturated or unsaturated  
heterocyclic group containing 2 to 4 carbon atoms and 0 to 2 additional  
nitrogen atoms wherein said saturated or unsaturated heterocyclic group is  
fused to a heterocyclic ring selected from the group consisting of dioxolane,  
dioxane, homodioxane, oxetane, tetrahydrofuran, dihydropyran, furan,  
25 oxazolidine, oxazole, isoxazole, oxazolidinone, oxathiolane, and 1,3-  
dioxolan-2-one and wherein the resulting fused ring is optionally substituted,  
in addition to the R<sup>2</sup> group, on any ring atom capable of substitution with 1 or  
2 substituents selected from the group consisting of alkyl, alkoxy, substituted  
alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or  
30 dialkylamino.

16. The compound of Claim 15 wherein B is 2-pyridone or 6-pyrimidone that  
is fused to a heterocyclic ring selected from the group consisting of  
dioxolane, dioxane, homodioxane, oxetane, tetrahydrofuran, dihydropyran,

5 furan, oxazolidine, oxazole, isoxazole, oxazolidinone, oxathiolane, and 1,3-  
dioxolan-2-one, and wherein the resulting fused ring is optionally substituted,  
in addition to the  $R^2$  group, on any ring atom capable of substitution with 1 or  
2 substituents selected from the group consisting of alkyl, alkoxy, substituted  
alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or  
10 dialkylamino.

17. The compound of Claim 11 to 16 wherein  $Ar^2$  is phenyl.

18. The compound of Claim 11 to 16 wherein X is hydroxyl and  $R^1$  is  
15 hydrogen.

19. The compound of Claim 18 wherein X is hydroxyl and  $R^1$  is hydrogen.

20. A method for treating a disease mediated by VLA-4 in a patient, which  
method comprises administering a pharmaceutical composition comprising a  
pharmaceutically acceptable carrier and a therapeutically effective amount of  
a compound of Claims 1 to 19.

21. A pharmaceutical composition comprising a pharmaceutically acceptable  
25 carrier and a therapeutically effective amount of a compound of Claims 1-19.

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